#### **CLAIMS**

1. A quinazoline derivative of the formula I:

$$A \longrightarrow \begin{pmatrix} R^6 & R^4 & R^2 \\ N & R^{5a} & R^2 \\ (R^1)_m & N \end{pmatrix}$$

wherein:

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m is 0, 1 or 2;

each  $\mathbb{R}^1$ , which may be the same or different, is selected from hydroxy, (1-6C)alkoxy, (3-7C)cycloalkyl-oxy and (3-7C)cycloalkyl-(1-6C)alkoxy,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a R<sup>1</sup> substituent optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents, or a substituent selected from hydroxy and (1-6C)alkoxy,

R<sup>2</sup> is hydrogen or (1-4C)alkyl;

**n** is 0, 1, 2, 3 or 4;

each R<sup>3</sup>, which may be the same or different, is selected from cyano, halogeno, (1-4C)alkyl, trifluoromethyl, (1-4C)alkoxy, (2-4C)alkenyl and (2-4C)alkynyl;

 $X^1$  is selected from O, S, SO, SO<sub>2</sub>, N(R<sup>7</sup>), CH(OR<sup>7</sup>), CON(R<sup>7</sup>), N(R<sup>7</sup>)CO, SO<sub>2</sub>N(R<sup>7</sup>), N(R<sup>7</sup>)SO<sub>2</sub>, OC(R<sup>7</sup>)<sub>2</sub>, C(R<sup>7</sup>)<sub>2</sub>O, SC(R<sup>7</sup>)<sub>2</sub>, C(R<sup>7</sup>)<sub>2</sub>S, CO, C(R<sup>7</sup>)<sub>2</sub>N(R<sup>7</sup>) and N(R<sup>7</sup>)C(R<sup>7</sup>)<sub>2</sub>, wherein each R<sup>7</sup>, which may be the same or different, is hydrogen or (1-6C)alkyl;

 $Q^1$  is aryl, or heteroaryl,

and wherein Q<sup>1</sup> optionally bears one or more substituents, which may be the same or different, selected from halogeno, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, sulfamoyl, formyl, mercapto, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl,

25 (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, NN-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (3-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino,

 $\underline{N}$ -(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino,  $\underline{N}$ -(1-6C)alkyl-(3-6C)alkynoylamino,  $\underline{N}$ -(1-6C)alkyl-(3-6C)alkynoylamino,  $\underline{N}$ -(1-6C)alkylsulfamoyl,  $\underline{N}$ - $\underline{N}$ -(1-6C)alkylsulfamoyl,  $\underline{N}$ - $\underline{N}$ -(1-6C)alkyl-(1-6C)alkanesulfonylamino, and a group of the formula:

 $-X^2-R^8$ 

wherein  $X^2$  is a direct bond or is selected from O, CO and N(R<sup>9</sup>), wherein R<sup>9</sup> is hydrogen or (1-6C)alkyl, and R<sup>8</sup> is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, carboxy-(1-6C)alkyl, (1-6C)alkyl, (1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)a

10 (2-6C)alkanoylamino-(1-6C)alkyl, <u>N</u>-(1-6C)alkyl-(2-6C)alkanoylamino-(1-6C)alkyl, (1-6C)alkoxycarbonylamino-(1-6C)alkyl, carbamoyl-(1-6C)alkyl, <u>N</u>-(1-6C)alkylcarbamoyl-(1-6C)alkyl, <u>N,N</u>-di-[(1-6C)alkyl]carbamoyl-(1-6C)alkyl, (1-6C)alkylthio-(1-6C)alkyl, (1-6C)alkylsulfinyl-(1-6C)alkyl, (1-6C)alkylsulfonyl-(1-6C)alkylsulfamoyl(1-6C)alkyl, <u>N,N</u>-

di-(1-6C)alkylsulfamoyl(1-6C)alkyl, (2-6C)alkanoyl-(1-6C)alkyl, (2-6C)alkanoyloxy-(1-6C)alkyl or (1-6C)alkoxycarbonyl-(1-6C)alkyl,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within -X<sup>1</sup>-Q<sup>1</sup> optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, amino, (1-4C)alkoxy, (1-4C)alkylamino and di-[(1-4C)alkylamino];

20  $R^4$ ,  $R^{4a}$ ,  $R^5$  and  $R^{5a}$ , which may be the same or different, are selected from hydrogen and (1-6C)alkyl, or

R<sup>4</sup> and R<sup>4a</sup> together with the carbon atom to which they are attached form a (3-7C)cycloalkyl ring, or

R<sup>5</sup> and R<sup>5a</sup> together with the carbon atom to which they are attached form a (3-25 7C)cycloalkyl ring,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within any of R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup> and R<sup>5a</sup> optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno substituents or a substituent selected from hydroxy, cyano, (1-6C)alkoxy, amino, (2-6C)alkanoyl, (1-6C)alkylamino and di-[(1-6C)alkylamino];

R<sup>6</sup> is selected from hydrogen, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl and heterocyclyl-(1-6C)alkyl,

and wherein any heterocyclyl group within an R<sup>6</sup> substituent optionally bears one or more substituents, which may be the same or different, selected from halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, formyl, mercapto, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (2-6C)alkanoyl, (2-6C)alkanoyloxy and from a group of the formula:

$$-X^{3}-R^{10}$$

wherein X<sup>3</sup> is a direct bond or is selected from O, CO, SO<sub>2</sub> and N(R<sup>11</sup>), wherein R<sup>11</sup> is hydrogen or (1-4C)alkyl, and R<sup>10</sup> is halogeno-(1-4C)alkyl, hydroxy-(1-4C)alkyl,

10 (1-4C)alkoxy-(1-4C)alkyl, cyano-(1-4C)alkyl, amino-(1-4C)alkyl,

 $\underline{N}$ -(1-4C)alkylamino-(1-4C)alkyl and  $\underline{N}$ -di-[(1-4C)alkyl]amino-(1-4C)alkyl,

and wherein any heterocyclyl group within an R<sup>6</sup> substituent optionally bears 1 or 2 oxo or thioxo substituents;

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a R<sup>6</sup> substituent, other than a CH<sub>2</sub> group

15 within a heterocyclyl group, optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more
halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, amino,
carboxy, carbamoyl, sulfamoyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio,
(1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino,
N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl,

20 (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino;

A is selected from hydrogen, a group of the formula Z- $(CR^{12}R^{13})_p$ - and  $R^{14}$ , wherein p is 1, 2, 3, or 4,

each R<sup>12</sup> and R<sup>13</sup>, which may be the same or different, is selected from hydrogen, (1-6C)alkyl, (2-6C)alkenyl and (2-6C)alkynyl,

or an R<sup>12</sup> and an R<sup>13</sup> group attached to the same carbon atom form a (3-7C)cycloalkyl or (3-7C)cycloalkenyl ring,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within any of R<sup>12</sup> and R<sup>13</sup>, optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, (1-6C)alkyl, (1-6C)alkoxy, amino, (2-6C)alkanoyl, (1-6C)alkylamino and di-[(1-6C)alkyl]amino,

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Z is selected from hydrogen, OR<sup>15</sup>, NR<sup>16</sup>R<sup>17</sup>, (1-6C)alkylsulfonyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, wherein each of R<sup>15</sup>, R<sup>16</sup> and R<sup>17</sup>, which may be the same or different, is selected from hydrogen, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl and (1-6C)alkoxycarbonyl,

or Z is a group of the formula:

$$O^2-X^4-$$

wherein  $X^4$  is selected from O,  $N(R^{18})$ ,  $SO_2$  and  $SO_2N(R^{18})$ , wherein  $R^{18}$  is hydrogen or (1-6C)alkyl, and  $Q^2$  is (3-7C)cycloalkyl, (3-7C)cycloalkenyl or heterocyclyl,

R<sup>14</sup> is selected from hydrogen, OR<sup>19</sup> and NR<sup>16</sup>R<sup>17</sup>, wherein R<sup>19</sup> is selected from (1-10 6C)alkyl, (2-6C)alkenyl and (2-6C)alkynyl, and wherein R<sup>16</sup> and R<sup>17</sup> are as defined above, or R<sup>14</sup> is a group of the formula:

$$Q^3-X^5-$$

wherein  $X^5$  is selected from O and  $N(R^{20})$ , wherein  $R^{20}$  is hydrogen or (1-6C)alkyl, and  $Q^3$  is (3-7C)cycloalkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl, (3-7C)cycloalkenyl,

15 (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl and heterocyclyl-(1-6C)alkyl, or R<sup>14</sup> is Q<sup>4</sup> wherein Q<sup>4</sup> is (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein adjacent carbon atoms in any (2-6C)alkylene chain within a Z or R<sup>14</sup>
20 substituent are optionally separated by the insertion into the chain of a group selected from O, S, SO, SO<sub>2</sub>, N(R<sup>21</sup>), CO, -C=C- and -C≡C-, wherein R<sup>21</sup> is hydrogen or (1-6C)alkyl, and wherein any heterocyclyl group within a Z or R<sup>14</sup> substituent optionally bears

and wherein any heterocyclyl group within a Z or R<sup>2+</sup> substituent optionally bears one or more substituents, which may be the same or different, selected from halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, formyl, mercapto, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (2-6C)alkanoyl, (2-6C)alkanoyloxy and from a group of the formula:

$$-X^{6}-R^{22}$$

wherein X<sup>6</sup> is a direct bond or is selected from O, CO, SO<sub>2</sub> and N(R<sup>23</sup>), wherein R<sup>23</sup> is hydrogen or (1-4C)alkyl, and R<sup>22</sup> is halogeno-(1-4C)alkyl, hydroxy-(1-4C)alkyl, (1-4C)alkoxy-(1-4C)alkyl, cyano-(1-4C)alkyl, amino-(1-4C)alkyl, N-(1-4C)alkylamino-(1-4C)alkyl and N,N-di-[(1-4C)alkyl]amino-(1-4C)alkyl,

and wherein any heterocyclyl group within a Z or  $R^{14}$  substituent optionally bears 1 or 2 oxo or thioxo substituents,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a Z or R<sup>14</sup> group, other than a CH<sub>2</sub> group within a heterocyclyl ring, optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more

5 halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, amino, carboxy, carbamoyl, sulfamoyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino; or a pharmaceutically acceptable salt thereof.

- 2. A quinazoline derivative according to claim 1, wherein:
- 15 m is 0, 1 or 2;

each R<sup>1</sup>, which may be the same or different, is selected from hydroxy, (1-6C)alkoxy, (3-7C)cycloalkyl-oxy and (3-7C)cycloalkyl-(1-6C)alkoxy,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a R<sup>1</sup> substituent optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents, or a substituent 20 selected from hydroxy and (1-6C)alkoxy,

R<sup>2</sup> is hydrogen or (1-4C)alkyl;

n is 0, 1, 2, 3 or 4;

each R<sup>3</sup>, which may be the same or different, is selected from halogeno, (1-4C)alkyl, trifluoromethyl, (1-4C)alkoxy, (2-4C)alkenyl and (2-4C)alkynyl;

 $X^1$  is selected from O, S, SO, SO<sub>2</sub>, N(R<sup>7</sup>), CH(OR<sup>7</sup>), CON(R<sup>7</sup>), N(R<sup>7</sup>)CO, SO<sub>2</sub>N(R<sup>7</sup>), N(R<sup>7</sup>)SO<sub>2</sub>, OC(R<sup>7</sup>)<sub>2</sub>, C(R<sup>7</sup>)<sub>2</sub>O, SC(R<sup>7</sup>)<sub>2</sub>, C(R<sup>7</sup>)<sub>2</sub>S, CO, C(R<sup>7</sup>)<sub>2</sub>N(R<sup>7</sup>) and N(R<sup>7</sup>)C(R<sup>7</sup>)<sub>2</sub>, wherein each R<sup>7</sup>, which may be the same or different, is hydrogen or (1-6C)alkyl;

Q<sup>1</sup> is aryl, or heteroaryl,

and wherein Q<sup>1</sup> optionally bears one or more substituents, which may be the same or different, selected from halogeno, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, sulfamoyl, formyl, mercapto, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl,

 $\underline{N}$ -(1-6C)alkylcarbamoyl,  $\underline{N}$ -di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (3-6C)alkenoyl, (3-6C)alkynoyl, (2-6C)alkanoyloxy, (2-6C)alkanoyloxy, (2-6C)alkanoyloxy,

 $\underline{N}$ -(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino,  $\underline{N}$ -(1-6C)alkyl-(3-

6C) alkenoylamino, (3-6C) alkynoylamino, N-(1-6C) alkyl-(3-6C) alkynoylamino,

5 N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, and a group of the formula:

$$-X^2-R^8$$

wherein  $X^2$  is a direct bond or is selected from O, CO and  $N(R^9)$ , wherein  $R^9$  is hydrogen or (1-6C)alkyl, and  $R^8$  is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, carboxy-(1-6C)alkyl, carboxy-(1-6C)alkyl,

10 6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl,  $\underline{N}$ -

(1-6C)alkylamino-(1-6C)alkyl, N,N-di-(1-6C)alkyl]amino-(1-6C)alkyl,

(2-6C)alkanoylamino-(1-6C)alkyl, N-(1-6C)alkyl-(2-6C)alkanoylamino-(1-6C)alkyl,

(1-6C)alkoxycarbonylamino-(1-6C)alkyl, carbamoyl-(1-6C)alkyl,

 $\underline{N}$ -(1-6C)alkylcarbamoyl-(1-6C)alkyl,  $\underline{N}$ -di-[(1-6C)alkyl]carbamoyl-(1-6C)alkyl, (1-6C)alkyl)

15 6C)alkylthio-(1-6C)alkyl, (1-6C)alkylsulfinyl-(1-6C)alkyl, (1-6C)alkylsulfonyl-(1-6C)alkylsulfamoyl(1-6C)alkyl, NN-(1-6C)alkylsulfamoyl(1-6C)alkyl, NN-di-(1-6C)alkylsulfamoyl(1-6C)alkyl, (2-6C)alkanoyl-(1-6C)alkyl, (2-6C)alkanoyl-(1-6C)alkyl, (2-6C)alkyl, (2-6C)alkyl, (2-6C)alkyl, (2-6C)alkyl, (2-6C)alkyl,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within -X<sup>1</sup>-Q<sup>1</sup> optionally bears on each said CH<sub>2</sub>

20 or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, amino, (1-4C)alkoxy, (1-4C)alkylamino and di-[(1-4C)alkylamino];

 $R^4$ ,  $R^{4a}$ ,  $R^5$  and  $R^{5a}$ , which may be the same or different, are selected from hydrogen and (1-6C)alkyl, or

R<sup>4</sup> and R<sup>4a</sup> together with the carbon atom to which they are attached form a (3-7C)cycloalkyl ring, or

 $m R^5$  and  $m R^{5a}$  together with the carbon atom to which they are attached form a (3-7C)cycloalkyl ring,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within any of R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup> and R<sup>5a</sup> optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno substituents or a substituent selected from hydroxy, cyano, (1-6C)alkoxy, amino, (2-6C)alkanoyl, (1-6C)alkylamino and di-[(1-6C)alkylamino];

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R<sup>6</sup> is selected from hydrogen, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl and heterocyclyl-(1-6C)alkyl,

and wherein any heterocyclyl group within an R<sup>6</sup> substituent optionally bears one or more substituents, which may be the same or different, selected from halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, formyl, mercapto, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (2-6C)alkanoyl, (2-6C)alkanoyloxy and from a group of the formula:

 $-X^{3}-R^{10}$ 

wherein  $X^3$  is a direct bond or is selected from O, CO, SO<sub>2</sub> and N(R<sup>11</sup>), wherein R<sup>11</sup> is hydrogen or (1-4C)alkyl, and R<sup>10</sup> is halogeno-(1-4C)alkyl, hydroxy-(1-4C)alkyl, (1-4C)alkyl, cyano-(1-4C)alkyl, amino-(1-4C)alkyl, M-(1-4C)alkyl and N.N-di-[(1-4C)alkyl]amino-(1-4C)alkyl,

and wherein any heterocyclyl group within an R<sup>6</sup> substituent optionally bears 1 or 2 oxo or thioxo substituents;

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a R<sup>6</sup> substituent, other than a CH<sub>2</sub> group within a heterocyclyl group, optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, amino, carboxy, carbamoyl, sulfamoyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanoylamino and N-(1-6C)alkyl-(1-6C)alkanosulfonylamino;

A is selected from hydrogen, a group of the formula Z- $(CR^{12}R^{13})_{p}$ - and  $R^{14}$ , wherein p is 1, 2, 3, or 4,

each R<sup>12</sup> and R<sup>13</sup>, which may be the same or different, is selected from hydrogen, (1-6C)alkyl, (2-6C)alkenyl and (2-6C)alkynyl,

or an R<sup>12</sup> and an R<sup>13</sup> group attached to the same carbon atom form a (3-7C)cycloalkyl or (3-7C)cycloalkenyl ring,

and wherein any  $CH_2$  or  $CH_3$  group within any of  $R^{12}$  and  $R^{13}$ , optionally bears on each said  $CH_2$  or  $CH_3$  group one or more halogeno or (1-6C)alkyl substituents or a substituent

selected from hydroxy, cyano, (1-6C)alkyl, (1-6C)alkoxy, amino, (2-6C)alkanoyl, (1-6C)alkylamino and di-[(1-6C)alkyl]amino,

Z is selected from hydrogen, OR<sup>15</sup>, NR<sup>16</sup>R<sup>17</sup>, (1-6C)alkylsulfonyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, wherein each of R<sup>15</sup>, R<sup>16</sup> and R<sup>17</sup>, which may be the same or different, is selected from hydrogen, (1-6C)alkyl, (2-6C)alkenyl and (2-6C)alkynyl,

or Z is a group of the formula:

$$Q^2-X^4-$$

wherein  $X^4$  is selected from O,  $N(R^{18})$ ,  $SO_2$  and  $SO_2N(R^{18})$ , wherein  $R^{18}$  is hydrogen or (1-6C)alkyl, and  $Q^2$  is (3-7C)cycloalkyl, (3-7C)cycloalkenyl or heterocyclyl,

R<sup>14</sup> is selected from hydrogen, OR<sup>19</sup> and NR<sup>16</sup>R<sup>17</sup>, wherein R<sup>19</sup> is selected from (1-6C)alkyl, (2-6C)alkenyl and (2-6C)alkynyl, and wherein R<sup>16</sup> and R<sup>17</sup> are as defined above, or R<sup>14</sup> is a group of the formula:

$$Q^{3}-X^{5}-$$

wherein X<sup>5</sup> is selected from O and N(R<sup>20</sup>), wherein R<sup>20</sup> is hydrogen or (1-6C)alkyl, and Q<sup>3</sup> is (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl and heterocyclyl-(1-6C)alkyl,

or R<sup>14</sup> is Q<sup>4</sup> wherein Q<sup>4</sup> is (3-7C)cycloalkyl, (3-7C)cycloalkenyl or heterocyclyl, and wherein adjacent carbon atoms in any (2-6C)alkylene chain within a Z or R<sup>14</sup>

substituent are optionally separated by the insertion into the chain of a group selected from O, S, SO, SO<sub>2</sub>,  $N(R^{21})$ , CO, -C=C- and -C $\equiv$ C-, wherein  $R^{21}$  is hydrogen or (1-6C)alkyl,

and wherein any heterocyclyl group within a Z or R<sup>14</sup> substituent optionally bears one or more substituents, which may be the same or different, selected from halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, formyl, mercapto, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (2-6C)alkanoyl, (2-6C)alkanoyloxy and from a group of the formula:

$$-X^{6}-R^{22}$$

wherein X<sup>6</sup> is a direct bond or is selected from O, CO, SO<sub>2</sub> and N(R<sup>23</sup>), wherein R<sup>23</sup> is hydrogen or (1-4C)alkyl, and R<sup>22</sup> is halogeno-(1-4C)alkyl, hydroxy-(1-4C)alkyl, (1-4C)alkyl, cyano-(1-4C)alkyl, amino-(1-4C)alkyl, M-(1-4C)alkylamino-(1-4C)alkyl and N,N-di-[(1-4C)alkyl]amino-(1-4C)alkyl,

and wherein any heterocyclyl group within a Z or  $R^{14}$  substituent optionally bears 1 or 2 oxo or thioxo substituents,

and wherein any  $CH_2$  or  $CH_3$  group within a Z or  $R^{14}$  group, other than a  $CH_2$  group within a heterocyclyl ring, optionally bears on each said  $CH_2$  or  $CH_3$  group one or more

- 5 halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, amino, carboxy, carbamoyl, sulfamoyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, N-(1-6C)alkylcarbamoyl, NN-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino,
- 10 N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino; or a pharmaceutically acceptable salt thereof.
- 3. A quinazoline derivative according to claim 1 or claim 2, wherein R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup> and R<sup>5a</sup>, which may be the same or different, are selected from hydrogen and (1-6C)alkyl, and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within any of R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup> and R<sup>5a</sup> optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno substituents or a substituent selected from hydroxy, cyano, (1-6C)alkoxy, amino, (2-6C)alkanoyl, (1-6C)alkylamino and di-[(1-6C)alkylamino].
- 20 4. A quinazoline derivative according to any one of the preceding claims, wherein m is 0.
  - 5. A quinazoline derivative according to any one of the preceding claims, wherein R<sup>2</sup> is hydrogen.
- 25 6. A quinazoline derivative according to any one of the preceding claims, wherein n is 0, 1 or 2 and, when present, at least one R<sup>3</sup> is in-a-meta-position (3-position) relative to the nitrogen of the anilino group in formula I.
- 7. A quinazoline derivative according to any one of the preceding claims, wherein n is 1 30 and R<sup>3</sup> is selected from halogeno and (1-4C)alkyl.
  - 8. A quinazoline derivative according to claim 7, wherein R<sup>3</sup> is chloro.

- 9. A quinazoline derivative according to claim 7, wherein R<sup>3</sup> is methyl.
- 10. A quinazoline derivative according to any one of the preceding claims, wherein X¹ is selected from O, S, OC(R³)2, SC(R³)2, SO, SO2, N(R³), CO and N(R³)C(R³)2 wherein each
  5 R³, which may be the same or different, is selected from hydrogen or (1-6C)alkyl.
  - 11. A quinazoline derivative according to any one of the preceding claims, wherein  $X^1$  is selected from O, S and  $OC(R^7)_2$  wherein each  $R^7$  is, independently, hydrogen or (1-4C)alkyl.
- 10 12. A quinazoline derivative according to any one of the preceding claims, wherein  $X^1$  is OCH<sub>2</sub>.
- 13. A quinazoline derivative according to any one of the preceding claims, wherein Q<sup>1</sup> is selected from phenyl and a 5- or 6-membered monocyclic heteroaryl ring, which ring contains
   15. 1, 2 or 3 heteroatoms independently selected from oxygen, nitrogen and sulfur,

and wherein Q<sup>1</sup> optionally bears one or more substituents, which may be the same or different, selected from halogeno, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, sulfamoyl, formyl, mercapto, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl,

- 20 (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (3-6C)alkenoyl, (3-6C)alkynoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)
- 6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino,

  N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino,
  N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, and a group of the formula:

 $-X^{2}-R^{8}$ 

wherein X<sup>2</sup> is a direct bond or is selected from O, CO and N(R<sup>9</sup>), wherein R<sup>9</sup> is hydrogen or (1-6C)alkyl, and R<sup>8</sup> is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, carboxy-(1-30 6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, N-(1-6C)alkyl, N-di-[(1-6C)alkyl]amino-(1-6C)alkyl,

(2-6C)alkanoylamino-(1-6C)alkyl, N-(1-6C)alkyl-(2-6C)alkanoylamino-(1-6C)alkyl, (1-6C)alkoxycarbonylamino-(1-6C)alkyl, carbamoyl-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, (1-6C)alkyl, (1-6C)alkyl, (1-6C)alkyl, (1-6C)alkyl, (1-6C)alkyl, (1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, N-(1-6C)alkyl, (2-6C)alkyl, (2-6C)alky

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within -X<sup>1</sup>-Q<sup>1</sup> optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from 10 hydroxy, cyano, amino, (1-4C)alkoxy, (1-4C)alkylamino and di-[(1-4C)alkylamino].

14. A quinazoline derivative according to any one of the preceding claims, wherein Q<sup>1</sup> is selected from phenyl, pyridyl, pyrazinyl, 1,3-thiazolyl, 1H-imidazolyl, 1H-pyrazolyl, 1,3-oxazolyl and isoxazolyl.

15

15. A quinazoline derivative according to any one of the preceding claims, wherein R<sup>6</sup> is selected from hydrogen, (1-3C)alkyl, (2-3C)alkenyl, (2-3C)alkynyl, (3-5C)cycloalkyl, (3-5C)cycloalkyl, (4-3C)alkyl, heterocyclyl and heterocyclyl-(1-3C)alkyl,

wherein any heterocyclyl group within R<sup>6</sup> is a 4, 5, 6 or 7 membered monocyclic

saturated or partially saturated heterocyclyl ring containing 1 or 2 heteroatoms selected from oxygen, nitrogen and sulfur, which heterocyclyl group is linked to the group to which it is attached by a ring carbon atom,

and wherein any heterocyclyl group within an R<sup>6</sup> substituent optionally bears one or more substituents, which may be the same or different, selected from halogeno,

trifluoromethyl, cyano, nitro, hydroxy, amino, mercapto, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (2-6C)alkanoyl, (2-6C)alkanoyloxy and from a group of the formula:

$$-X^{3}-R^{10}$$

wherein X<sup>3</sup> is a direct bond or is selected from O and N(R<sup>11</sup>), wherein R<sup>11</sup> is hydrogen or (1-4C)alkyl, and R<sup>10</sup> is halogeno-(1-4C)alkyl, hydroxy-(1-4C)alkyl,

(1-4C)alkoxy-(1-4C)alkyl, cyano-(1-4C)alkyl, amino-(1-4C)alkyl,

 $\underline{N}$ -(1-4C)alkylamino-(1-4C)alkyl and  $\underline{N}$ -di-[(1-4C)alkyl]amino-(1-4C)alkyl,

and wherein any heterocyclyl group within an R<sup>6</sup> substituent optionally bears 1 or 2 oxo substituents;

- and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a R<sup>6</sup> substituent, other than a CH<sub>2</sub> group within a heterocyclyl group, optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, amino, (1-6C)alkoxy, (1-6C)alkylamino and di-[(1-6C)alkyl]amino.
- 10 16. A quinazoline derivative according to claim 15, wherein R<sup>6</sup> is (1-3C)alkyl, and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a R<sup>6</sup> substituent, other than a CH<sub>2</sub> group within a heterocyclyl group, optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, amino, (1-6C)alkoxy, (1-6C)alkylamino and di-[(1-6C)alkyl]amino.

15

17. A quinazoline derivative according to any one of the preceding claims, wherein A is selected from a group of the formula Z- $(CR^{12}R^{13})_{p}$ - and  $R^{14}$ ,

wherein p is 1, 2 or 3,

each R<sup>12</sup> and R<sup>13</sup>, which may be the same or different, is selected from hydrogen and 20 (1-6C)alkyl,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within any of R<sup>12</sup> and R<sup>13</sup> optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno substituents or a substituent selected from hydroxy and (1-6C)alkoxy,

Z is selected from hydrogen, OR<sup>15</sup>, NR<sup>16</sup>R<sup>17</sup> and (1-6C)alkylsulfonyl, wherein each of 25 R<sup>15</sup>, R<sup>16</sup> and R<sup>17</sup>, which may be the same or different, is selected from hydrogen, (1-6C)alkyl and (1-6C)alkoxycarbonyl,

 $R^{14}$  is selected from  $OR^{19}$  and  $NR^{16}R^{17}$ , wherein  $R^{19}$  is selected from (1-6C)alkyl and wherein  $R^{16}$  and  $R^{17}$  are as defined above,

or  $\mathbb{R}^{14}$  is  $\mathbb{Q}^4$  wherein  $\mathbb{Q}^4$  is (3-7C)cycloalkyl, heterocyclyl or heterocyclyl-(1-30 6C)alkyl,

and wherein any heterocyclyl group within a Z or R<sup>14</sup> substituent optionally bears one or more substituents, which may be the same or different, selected from halogeno, hydroxy, (1-6C)alkyl and (1-6C)alkoxy,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a Z or R<sup>14</sup> group, other than a CH<sub>2</sub> group within a heterocyclyl ring, optionally bears on each said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy and (1-6C)alkoxy.

5

- 18. A quinazoline derivative selected from one or more of the following:
- $N-\{2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]ethyl\}-2-methoxy-N-methylacetamide;$
- $N-\{2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy] ethyl\}-2-independent of the property of the property$
- 10 (dimethylamino)-N-methylacetamide;
  - $N-\{(2R)-2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]$ propyl $\}-2-methoxy-N-methylacetamide);$
  - 2-hydroxy-N-methyl-N-{2-[(4-{3-methyl-4-(pyrazin-2-ylmethoxy)anilino}quinazolin-5-yl)oxy]ethyl}acetamide;
- 2-hydroxy-N-methyl-N-{2-[(4-{3-methyl-4-(1,3-thiazol-4-ylmethoxy)anilino}quinazolin-5-yl)oxy]ethyl}acetamide;
  - $2-hydroxy-N-methyl-N-(2-\{[4-(3-methyl-4-[(5-methylisoxazol-3-methyl-4-(5-methyl-4-(5-methylisoxazol-3-methylisoxazol-3-methylisoxazol-3-(5-methylisoxazol-3-methylisoxazol-3-(5-methylisoxazol-3-methylisoxazol-3-(5-methylisoxazol-3-methylisoxazol-3-(5-methylisoxazol-3-methylis$
  - yl)methoxy]anilino)quinazolin-5-yl]oxy}ethyl)acetamide;
  - $N-\{(2R)-2-[(4-\{3-\text{chloro-}4-(\text{pyridin-}2-\text{ylmethoxy})\text{anilino}\}\text{quinazolin-}5-\text{yl})\text{oxy}]\text{propyl}\}-2-[(4-\{3-\text{chloro-}4-(\text{pyridin-}2-\text{ylmethoxy})\text{anilino}\}\text{quinazolin-}5-\text{yl})\text{oxy}]\text{propyl}\}-2-[(4-\{3-\text{chloro-}4-(\text{pyridin-}2-\text{ylmethoxy})\text{anilino}\}\text{quinazolin-}5-\text{yl})\text{oxy}]\text{propyl}\}-2-[(4-\{3-\text{chloro-}4-(\text{pyridin-}2-\text{ylmethoxy})\text{anilino}\}\text{quinazolin-}5-\text{yl})\text{oxy}]\text{propyl}]$
- 20 methoxyacetamide;
  - $N-(2-\{[4-(3-chloro-4-[(6-methylpyridin-2-yl)methoxy]anilino)$ quinazolin-5-yl]oxy $\}$ ethyl)-2-hydroxy-N-methylacetamide;
  - N-((2R)-2-{[4-(3-chloro-4-[(6-methylpyridin-2-yl)methoxy]anilino)quinazolin-5-yl]oxy}propyl)-2-hydroxy-N-methylacetamide;
- 25 N-(2-{[4-(3-chloro-4-[(6-methylpyridin-2-yl)methoxy]anilino)quinazolin-5-yl]oxy}ethyl)-N-methylacetamide;
  - N-(2-{[4-(3-chloro-4-[(2-fluorobenzyl)oxy]anilino)quinazolin-5-yl]oxy}ethyl)-N-methylacetamide;
  - N-(2-{[4-(3-chloro-4-[(3-fluorobenzyl)oxy]anilino)quinazolin-5-yl]oxy}ethyl)-N-
- 30 methylacetamide;
  - $N-\{2-[(4-\{3-chloro-4-(1,3-thiazol-4-ylmethoxy)anilino\}quinazolin-5-yl)oxy]ethyl\}-N-methylacetamide;$

- $N-\{2-[(4-\{3-chloro-4-(pyrazin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]ethyl\}-N-methylacetamide;$
- $N-\{(2R)-2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]$ propyl $\}-2-hydroxyacetamide;$
- 5 *N*-{2-[(4-{3-chloro-4-(pyridin-2-ylmethoxy)anilino}quinazolin-5-yl)oxy]ethyl}-*N*-methylacetamide;
  - 2-hydroxy-N-methyl-N-{2-[(4-{3-methyl-4-(pyridin-2-ylmethoxy)anilino}quinazolin-5-yl)oxylethyl}acetamide;
  - $N-\{(1R)-2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-$
- 10 methylethyl}acetamide;
  - $N-\{(1R)-2-[(4-\{3-\text{chloro}-4-(\text{pyridin}-2-\text{ylmethoxy})\text{anilino}\}\text{quinazolin}-5-\text{yl})\text{oxy}]-1-\text{methylethyl}\}-2-\text{hydroxyacetamide};$
  - $N-\{2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]ethyl\}-2-hydroxy-N-methylacetamide;$
- 15 *N*-(2-{[4-(3-chloro-4-[(3-fluorobenzyl)oxy]anilino)quinazolin-5-yl]oxy}ethyl)-2-hydroxy-*N*-methylacetamide;
  - $N-\{2-[(4-\{3-chloro-4-(1,3-thiazol-4-ylmethoxy)anilino\}quinazolin-5-yl)oxy]ethyl\}-2-hydroxy-N-methylacetamide;$
- 20 N-methylacetamide;
  - $N-\{2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]ethyl\}$  acetamide;  $N-\{(2R)-2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]propyl\}$  acetamide;
  - $N-\{(2R)-2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]$ propyl $\}-2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]$
- 25 hydroxy-N-methylacetamide;
  - $N-\{(2R)-2-[(4-\{3-chloro-4-(pyrazin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]$  propyl $\}-2-hydroxy-N-methylacetamide;$
  - $N-((2R)-2-\{[4-(3-\text{chloro}-4-[(3-\text{fluorobenzyl})oxy]anilino)\text{quinazolin-5-yl}]oxy\}$ propyl)-2-hydroxy-N-methylacetamide;

- $N-\{(2R)-2-[(4-\{3-\text{chloro-}4-(1,3-\text{thiazol-}4-\text{ylmethoxy})\text{anilino}\}\text{quinazolin-}5-\text{yl})\text{oxy}]$  hydroxy-N-methylacetamide;
- $N-\{(2R)-2-[(4-\{3-chloro-4-(pyridin-2-ylmethoxy)anilino\}quinazolin-5-yl)oxy]$ propyl $\}-N-$ methylacetamide;
- 5  $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-ethylacetamide;$ 
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-ethyl-2-hydroxyacetamide;$
  - $\textit{N-}\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\} \\ quinazolin-5-yl) \\ oxy]ethyl\}-\textit{N-}\{1-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\}] \\ quinazolin-5-yl) \\ oxy]ethyl$
- 10 propylacetamide;
  - *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-2-hydroxy-*N*-propylacetamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-isopropylacetamide;$
- 15 *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-2-hydroxy-*N*-isopropylacetamide;
  - N-allyl-N-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}acetamide;
  - $N-\text{allyl-}N-\{2-[(4-\{[3-\text{chloro-}4-(\text{pyridin-}2-\text{ylmethoxy})\text{phenyl}]\text{amino}\}\text{quinazolin-}5-\text{pression}\}$
- 20 yl)oxy]ethyl}-2-hydroxyacetamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-cyclopropylacetamide;$
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-cyclopropyl-2-hydroxyacetamide;$
- 25 N-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-N-(cyclopropylmethyl)acetamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-(cyclopropylmethyl)-2-hydroxyacetamide;$
  - $\textit{N-}\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\} \\ \text{quinazolin-5-yl)} \\ \text{oxy}] \\ \text{ethyl}\}-\textit{N-}\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]} \\ \text{amino}\} \\ \text{quinazolin-5-yl)} \\ \text{oxy}] \\ \text{ethyl}\}-\textit{N-}\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]} \\ \text{amino}\} \\ \text{quinazolin-5-yl)} \\ \text{oxy}] \\ \text{ethyl}\}-\textit{N-}\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]} \\ \text{amino}\} \\ \text{quinazolin-5-yl)} \\ \text{oxy}] \\ \text{ethyl}\}-\textit{N-}\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]} \\ \text{quinazolin-5-yl)} \\ \text{oxy}] \\ \text{ethyl}\}-\textit{N-}\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]} \\ \text{quinazolin-5-yl)} \\ \text{oxy}] \\ \text{ethyl}] \\ \text{oxy}] \\ \text{ethyl}] \\ \text{oxy}] \\ \text{ethyl}] \\ \text{oxy}] \\ \text{ethyl}] \\ \text{oxy}] \\ \text{oxy}] \\ \text{ethyl}] \\ \text{oxy}] \\ \text{oxy}]$
- 30 cyclobutylacetamide;
  - *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-*N*-cyclobutyl-2-hydroxyacetamide;

- $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-(1-methylpiperidin-4-yl)acetamide;$
- $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-(tetrahydro-2H-pyran-4-yl)acetamide;$
- 5 *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-2-hydroxy-*N*-(tetrahydro-2*H*-pyran-4-yl)acetamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-(2-hydroxyethyl)acetamide;$
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-2-indin-2-ylmethoxylmetho$
- 10 hydroxy-N-(2-hydroxyethyl)acetamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-(2-methoxyethyl)acetamide;$
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-2-hydroxy-<math>N-(2-methoxyethyl)$ acetamide;
- 15 *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-*N*-prop-2-yn-1-ylacetamide;
  - *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-2-hydroxy-*N*-prop-2-yn-1-ylacetamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-2-indin-2-ylmethoxy amino phenyl]amino properties and the sum of the$
- 20 hydroxy-N-methylpropanamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N-methyl-tetrahydrofuranyl-2-carboxamide;$
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N,1-dimethylprolinamide;$
- 25 *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-2-hydroxy-*N*,2-dimethylpropanamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-1-hydroxy-<math>N$ -methylcyclopropanecarboxamide;
  - $N^1-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl]oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl]oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl]oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl]oxy]ethyl\}-\{1-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl]oxy]ethyl$
- 30  $N^1, N^2$ -dimethylglycinamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-3-hydroxy-<math>N$ ,2,2-trimethylpropanamide;

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- *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-3-hydroxy-*N*-methylpropanamide;
- N-{(2S)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]propyl}acetamide;
- 5 N-{(2\$)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]propyl}-2-hydroxyacetamide;
  - $N^{1}$ -{(2S)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy|propyl}- $N^{2}$ , $N^{2}$ -dimethylglycinamide;
- 10 yl)oxy]propyl}-2-methoxyacetamide;
  - $N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-ylmethoxy)$
  - yl)oxy]propyl}-2-(methylsulfonyl)acetamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-2-hydroxyacetamide;$
- 15  $N^1$ -{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}- $N^2$ , $N^2$ -dimethylglycinamide;
  - *N*-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-2-methoxyacetamide;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-2-indinazolin-5-yloxy]ethyl$
- 20 (methylsulfonyl)acetamide;
  - $N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\}$ quinazolin-5-
  - yl)oxy]propyl}-N-methylacetamide;
  - $\textit{N-}\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\} \\ \text{quinazolin-5-} \\ \text{pyridin-2-ylmethoxy} \\ \text{phenyl}]$
  - yl)oxy]propyl}-2-hydroxy-N-methylacetamide;
- 25  $N^1$ -{(2S)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]propyl}- $N^1$ , $N^2$ , $N^2$ -trimethylglycinamide;
  - $\textit{N-}\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\} \\ \text{quinazolin-5-}$
  - yl)oxy]propyl}-2-methoxy-N-methylacetamide;
  - N-{(2S)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-
- 30 yl)oxy]propyl}-N-methyl-2-(methylsulfonyl)acetamide;
  - $N-\{(2R)-2-[(4-\{[3-chloro-4-(pyrazin-2-ylmethoxy)phenyl]amino}\}$ quinazolin-5-yl)oxy]propyl $\}-N$ -methylacetamide;

- yl)oxy]propyl}-N-methylacetamide;
- N-((2R)-2-{[4-({3-chloro-4-[(3-fluorobenzyl)oxy]phenyl}amino)quinazolin-5-
- yl]oxy}propyl)-N-methylacetamide;
- 5 N-((2R)-2-{[4-({3-chloro-4-[(2-fluorobenzyl)oxy]phenyl}amino)quinazolin-5
  - $yl] oxy \} propyl) N methylacetamide; \\$
  - *N*-{(1*R*)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]-1-methylethyl}-2-hydroxy-*N*-methylacetamide;
  - $N-\{(1R)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]-1-$
- 10 methylethyl}-N-methylacetamide;
  - *N*-{(1*S*)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]-1-methylethyl}-2-hydroxy-*N*-methylacetamide;
  - *N*-{(1*S*)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]-1-methylethyl}-*N*-methylacetamide;
- 15 *N*-{(1*S*)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]-1-methylethyl}-2-methoxy-*N*-methylacetamide;
  - *N*-{(1*S*)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]-1-methylethyl}-2-hydroxyacetamide;
  - $N-\{(1S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl]oxy]-1-indinazolin-5-yl$
- 20 methylethyl}acetamide;
  - $N^1$ -{(1S)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]-1-methylethyl}- $N^2$ , $N^2$ -dimethylglycinamide;
  - $N^{1}$ -{(2R)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]propyl}- $N^{2}$ , $N^{2}$ -dimethylglycinamide;
- 25 (2S)-N-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-2,4-dihydroxybutanamide;
  - (2R)-N-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-2,4-dihydroxybutanamide;
  - $(2R)-N-\{(2R)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino]quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl]amino[pyridin-2-ylmethoxy)phenyl[py$
- 30 yl)oxy]propyl}-2,4-dihydroxybutanamide;
  - $(2S)-N-\{(2R)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]propyl\}-2,4-dihydroxybutanamide;$

- $(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-(hloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-(hloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-(hloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-\{[3-(hloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-[4-(hloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(2S)-2-[(4-[4-(hloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(4-[4-(hloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(2R)-N-\{(4-[4-(hloro-4-$
- yl)oxy]propyl}-2,4-dihydroxybutanamide;
- yl)oxy]propyl}-2,4-dihydroxybutanamide;
- 5 (2S)-N-{(1R)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]-1-methylethyl}-2,4-dihydroxybutanamide;
  - $(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]-1-methylethyl\}-2,4-dihydroxybutanamide;$
- 10 yl)oxy]ethyl}-2,4-dihydroxybutanamide;

  - yl)oxy]ethyl}-2,4-dihydroxybutanamide;
  - $(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino]\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino]\ quinazolin-5-(2R)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-(1$
  - yl)oxy]-1-methylethyl}-2,4-dihydroxybutanamide;
- 15  $(2S)-N-\{(1R)-2-[(4-\{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino}\}$  quinazolin-5
  - yl)oxy]-1-methylethyl}-2,4-dihydroxybutanamide;
  - N-methyl-N-{2-[(4-{[3-methyl-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}acetamide;
  - $N-\text{methyl-}N-\{2-[(4-\{[3-\text{methyl-}4-(1,3-\text{thiazol-}4-\text{ylmethoxy})\text{phenyl}]amino}\}\ quinazolin-5-(3-\text{methyl-}N-\{2-[(4-\{[3-\text{methyl-}4-(1,3-\text{thiazol-}4-\text{ylmethoxy})\text{phenyl}]amino}\}]$
- 20 yl)oxy]ethyl}acetamide;
  - N-methyl-N-(2-{[4-({3-methyl-4-[(5-methylisoxazol-3-yl)methoxy]phenyl}amino)
  - quinazolin-5-yl]oxy}ethyl)acetamide;
  - 2-hydroxy-N-methyl-N-{2-[(4-{[3-methyl-4-(1,3-thiazol-2-ylmethoxy)phenyl]
  - amino}quinazolin-5-yl)oxy]ethyl}acetamide;
- 25 2-hydroxy-N-{2-[(4-{[3-methyl-4-(pyridin-2-ylmethoxy)phenyl]amino} quinazolin-5-yl)oxy]ethyl}acetamide;
  - 2-hydroxy-*N*-{2-[(4-{[3-methyl-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino} quinazolin-5-yl)oxy]ethyl}acetamide;
  - $\textit{N-}\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\} \\ \text{quinazolin-5-yl}) \\ \text{oxy}]-1,1-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\} \\ \text{quinazolin-5-ylmethox}) \\ \text{quinazolin-5-ylmethox} \\ \text{quinazolin-6-ylmethox}) \\ \text{quinazolin-6-ylmethox} \\ \text{quinazolin-6-ylmethox}$
- 30 dimethylethyl}-2-hydroxyacetamide;
  - 2-hydroxy-N-{(2R)-2-[(4-{[3-methyl-4-(pyridin-2-ylmethoxy)phenyl]amino} quinazolin-5-yl)oxy]propyl}acetamide;

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2-hydroxy-N-{(2R)-2-[(4-{[3-methyl-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino} quinazolin-5-yl)oxy]propyl}acetamide;
N-((2R)-2-{[4-({4-[(3-fluorobenzyl)oxy]-3-methylphenyl}amino)quinazolin-5-yl]oxy}propyl)-2-hydroxyacetamide;
5 2-hydroxy-N-{(2R)-2-[(4-{[3-methyl-4-(1,3-thiazol-2-ylmethoxy)phenyl]amino} quinazolin-
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- 5 2-hydroxy-N-{(2R)-2-[(4-{[3-methyl-4-(1,3-thiazol-2-ylmethoxy)phenyl]amino} quinazolin-5-yl)oxy]propyl}acetamide;
  - $N-\{(2R)-2-[(4-\{[3-methyl-4-(pyridin-2-ylmethoxy)phenyl]amino}\}$ quinazolin-5-yl)oxy]propyl $\{$ acetamide $\}$
  - $N-\{(2R)-2-[(4-\{[3-methyl-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino\}quinazolin-5-ylmethoxy)$
- 10 yl)oxy]propyl}acetamide;
  - $N-((2R)-2-\{[4-(\{4-[(3-fluorobenzyl)oxy]-3-methylphenyl\}amino)quinazolin-5-yl]oxy\}$ propyl)acetamide;
  - $N-\{(2R)-2-[(4-\{[3-methyl-4-(1,3-thiazol-2-ylmethoxy)phenyl]amino}\}$ quinazolin-5-yl)oxy]propyl $\{acetamide;$
- 2-hydroxy-N-methyl-N-{(2R)-2-[(4-{[3-methyl-4-(pyridin-2-ylmethoxy)phenyl] amino}quinazolin-5-yl)oxy]propyl}acetamide;
  2-hydroxy-N-methyl-N-{(2R)-2-[(4-{[3-methyl-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]propyl}acetamide;
  2-hydroxy-N-methyl-N-((2R)-2-{[4-({3-methyl-4-[(5-methylisoxazol-3-
- yl)methoxy]phenyl}amino)quinazolin-5-yl]oxy}propyl)acetamide;
  N-methyl-N-{(1R)-1-methyl-2-[(4-{[3-methyl-4-(pyridin-2-ylmethoxy)phenyl]}
  amino}quinazolin-5-yl)oxy]ethyl}acetamide;
  N-methyl-N-{(1R)-1-methyl-2-[(4-{[3-methyl-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}acetamide;
- 25 N-{(1R)-2-[(4-{[3-chloro-4-(1,3-thiazol-4-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]-1-methylethyl}-2-hydroxy-N-methylacetamide;
  2-hydroxy-N-methyl-N-{(1R)-1-methyl-2-[(4-{[3-methyl-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}acetamide;
  - $2-hydroxy-N-methyl-N-\{(1R)-1-methyl-2-[(4-\{[3-methyl-4-(1,3-thiazol-4-(1,3-thia$
- 30 ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}acetamide;

  N-{(2R)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5yl)oxy]propyl}-1-hydroxy-N-methylcyclopropanecarboxamide;

- yl)oxy]propyl}-2-hydroxy-N-methylpropanamide;
- $N-\{(2R)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}\}$ quinazolin-5-
- yl)oxy]propyl}-2-hydroxy-N,2-dimethylpropanamide;
- - yl)oxy]propyl}-2-hydroxy-N-methylpropanamide;
  - $(2R)-N-\{(2R)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-(pyridin-2-ylmethoxy)phenyl]amino$
  - yl)oxylpropyl}-2-methoxy-N-methylpropanamide;
  - $2-hydroxy-N-methyl-N-((2R)-2-\{[4-(\{3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methyl-4-[(6-methyl-4-$
- 10 yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}propyl)acetamide;
  - $N-\text{methyl-}N-((2R)-2-\{[4-(\{3-\text{methyl-}4-[(6-\text{methylpyridin-}3-\text{yl})\text{oxy}]\text{phenyl}\}\text{amino})\text{quinazolin-}}$
  - 5-yl]oxy}propyl)acetamide;
  - $N^{1}$ ,  $N^{2}$ ,  $N^{2}$ -trimethyl- $N^{1}$ -((2R)-2-{[4-({3-methyl-4-[(6-methylpyridin-3-
  - yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}propyl)glycinamide;
- 15 N-methyl-N-((2R)-2-{[4-({3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl}amino)quinazolin-
  - 5-yl]oxy}propyl)-2-pyrrolidin-1-ylacetamide;
  - $\textit{N-}methyl-\textit{N-}((2R)-2-\{[4-(\{3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl\}amino)} quinazolin-2-((2R)-2-\{[4-(\{3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl\}amino)\} quinazolin-2-((2R)-2-\{[4-(\{3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl\}amino)\} quinazolin-2-((2R)-2-(\{3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl\}amino) quinazolin-2-((3-methylpyridin-3-yl)oxy]phenyl}$
  - 5-yl]oxy}propyl)-2-morpholin-4-ylacetamide;
  - N-methyl-N-((2R)-2-{[4-({3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl}amino)quinazolin-
- 20 5-yl]oxy}propyl)-2-(4-methylpiperazin-1-yl)acetamide;
  - $2-hydroxy-N-methyl-N-((2S)-2-\{[4-(\{3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methyl-4-[(6-methyl-4-$
  - yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}propyl)acetamide;
  - $N-\text{methyl-}N-((2S)-2-\{[4-(\{3-\text{methyl-}4-[(6-\text{methylpyridin-}3-\text{yl})oxy]phenyl}\} amino) quinazolin-leading and the state of the st$
  - 5-yl]oxy}propyl)acetamide;
- 25 *N*-methyl-*N*-((2*S*)-2-{[4-({3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}propyl)-2-pyrrolidin-1-ylacetamide;
  - (2S)-2,4-dihydroxy-N-((2R)-2-{[4-({3-methyl-4-[(6-methylpyridin-3-m
  - yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}propyl)butanamide;
  - (2S)-4-bromo-2-hydroxy-N-((2R)-2- $\{[4-(\{3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-met$
- 30 yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}propyl)butanamide;
  - N-(2-chloroethyl)-N'-((2R)-2-{[4-({3-methyl-4-[(6-methylpyridin-3-m
  - yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}propyl)urea;

- $2-hydroxy-N-methyl-N-((1R)-1-methyl-2-\{[4-(\{3-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methyl-4-[(6-methylpyridin-3-methyl-4-[(6-methyl-4-[(6-methyl-4-[(6-met$
- yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}ethyl)acetamide;
- N-methyl-N-((1R)-1-methyl-2-{[4-({3-methyl-4-[(6-methylpyridin-3-
- yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}ethyl)acetamide;
- 5 2-hydroxy-*N*-methyl-*N*-((1*S*)-1-methyl-2-{[4-({3-methyl-4-[(6-methylpyridin-3
  - yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}ethyl)acetamide;
  - N-methyl-N-((1S)-1-methyl-2-{[4-({3-methyl-4-[(6-methylpyridin-3-
  - yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}ethyl)acetamide;
  - methyl-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-
- 10 yl)oxy]ethyl}methylcarbamate;
  - $N-\{2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy]ethyl\}-N,N'-dimethylurea;$
  - N'-(2-chloroethyl)-N-{2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-N-methylurea;
- 15  $N-\{(2R)-2-[(4-\{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino\}quinazolin-5-yl)oxy[propyl]-<math>N$ -methylurea;
  - [((R)-2-{4-[3-chloro-4-(pyridin-2-ylmethoxy)phenylamino]quinazolin-5-
  - yloxy}propylcarbamoyl)methyl|methylcarbamic acid tert-butyl ester;
  - $N^{1}$ -{(2R)-2-[(4-{[3-chloro-4-(pyridin-2-ylmethoxy)phenyl]amino}quinazolin-5-
- 20 yl)oxy]propyl $-N^2$ -methylglycinamide;
  - 2-hydroxy-N-methyl-N-(2-{[4-({3-methyl-4-[(6-methylpyridin-3-
  - yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}ethyl)acetamide;
  - N-methyl-N-(2-{[4-({3-methyl-4-[(6-methylpyridin-3-yl)oxy]phenyl}amino)quinazolin-5-yl]oxy}ethyl)acetamide; and
- 25 N (2 F/4 (F2 ablama 4 (1 mastha
- 25 N-{2-[(4-{[3-chloro-4-(1-methyl-1-pyridin-2-ylethoxy)phenyl]amino}quinazolin-5-yl)oxy]ethyl}-N-methylacetamide;
  - or a pharmaceutically acceptable salt thereof.
  - 19. A pharmaceutical composition which comprises a quinazoline derivative of the
- 30 formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 18 in association with a pharmaceutically-acceptable diluent or carrier.

- 20. A quinazoline derivative of the formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 18 for use as a medicament.
- 21. A quinazoline derivative of the formula I, or a pharmaceutically acceptable salt
  5 thereof, as defined in any one of claims 1 to 18 for use in the production of an anti-proliferative effect which effect is produced alone or in part by inhibiting erbB2 receptor tyrosine kinase in a warm-blooded animal such as man.
- A quinazoline derivative of the formula I, or a pharmaceutically acceptable salt
   thereof, as defined in any one of claims 1 to 18 for use in the production of an erbB2 receptor tyrosine kinase inhibitory effect in a warm-blooded animal such as man.
- 23. A quinazoline derivative of the formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 18 for use in the production of a selective erbB2
   15 receptor tyrosine kinase inhibitory effect in a warm-blooded animal such as man.
  - 24. A process for the preparation of a quinazoline derivative of the formula I, or a pharmaceutically acceptable salt thereof, as defined in claim 1 which comprises:
- (a) the coupling, conveniently in the presence of a suitable base, of a quinazoline of the 20 formula  $\mathbf{II}$ :

$$R^{6}$$
 $R^{5}$ 
 $R^{4}$ 
 $R^{2}$ 
 $R^{3}$ 
 $R^{1}$ 
 $R^{3}$ 
 $R^{1}$ 
 $R^{1}$ 
 $R^{1}$ 

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^{4a}$ ,  $R^5$ ,  $R^{5a}$ ,  $R^6$ ,  $X^1$ ,  $Q^1$ , m, and n have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with a carboxylic acid of the formula  $\mathbf{III}$ , or a reactive derivative thereof:

## A-COOH

5

Ш

wherein A has any of the meanings defined in claim 1 except that any functional group is protected if necessary;

or

(b) for the preparation of those compounds of the formula I wherein X<sup>1</sup> is OC(R<sup>7</sup>)<sub>2</sub>,

SC(R<sup>7</sup>)<sub>2</sub> or N(R<sup>7</sup>)C(R<sup>7</sup>)<sub>2</sub>, the reaction, conveniently in the presence of a suitable base, of a quinazoline of the formula **IV**:

$$A \longrightarrow \begin{pmatrix} R^6 & R^4 & R^2 \\ N & R^5 & R^4 \\ N & (R^3)_n \end{pmatrix}$$

$$(R^1)_m$$

IV

wherein X<sup>1a</sup> is O, S or N(R<sup>7</sup>) and R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup>, R<sup>5a</sup>, R<sup>6</sup>, R<sup>7</sup>, A, m, and n have 15 any of the meanings defined in claim 1 except that any functional group is protected if necessary, with a compound of the formula V or a salt thereof:

$$Q^1$$
- $C(R^7)_2$ - $L^1$ 

V

wherein L<sup>1</sup> is a suitable displaceable group and Q<sup>1</sup> and R<sup>7</sup> have any of the meanings defined in claim 1 except that any functional group is protected if necessary;

(c) for the preparation of those compounds of the formula I wherein A is  $\mathbb{R}^{14}$  and  $\mathbb{R}^{14}$  is NHR<sup>17</sup> or  $\mathbb{Q}^3$ -X<sup>5</sup>- (wherein  $\mathbb{R}^{17}$  and  $\mathbb{Q}^3$  are as defined in claim 1 and X<sup>5</sup> is NH), the coupling of a quinazoline of the formula II as defined above in (a) with an isocyanate of the formula IIIa:

# A-NCO

# Шa

wherein A is R<sup>14</sup> as previously defined in this section except that any functional group is protected if necessary;

5 (d) the reaction of a quinazoline of the formula II wherein  $R^6$  is hydrogen:

П

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup>, R<sup>5a</sup>, X<sup>1</sup>, Q<sup>1</sup>, m, and n have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with α-hydroxy-10 γ-butyrolactone wherein any functional group is protected if necessary;

or

(e) the coupling of a quinazoline of the formula VI:

VI

wherein R<sup>1</sup>, R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup>, R<sup>5a</sup>, R<sup>6</sup>, A and m have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with a compound of the formula IIb:

$$R^2$$
 $N$ 
 $X^1$ 
 $Q^1$ 

wherein R<sup>2</sup>, R<sup>3</sup>, X<sup>1</sup>, Q<sup>1</sup> and n have any of the meanings defined in claim 1 except that any functional group is protected if necessary;

(f) for the preparation of those compounds of the formula I wherein X<sup>1</sup> is O and Q<sup>1</sup> is 2-pyridyl, 4-pyridyl, 2-pyrimidyl, 2-pyrazinyl or 3-pyridazinyl, the reaction, conveniently in the presence of a suitable base and a suitable catalyst, of a quinazoline of the 10 formula VII:

VII

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup>, R<sup>5a</sup>, R<sup>6</sup>, A, m and n have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with 2-bromopyridine, 4-bromopyridine, 2-chloropyrimidine, 2-chloropyrimidine, 2-chloropyridine; or

(g) for the preparation of those compounds of the formula I wherein A is Z-( $CR^{12}R^{13}$ )<sub>p</sub>-, wherein Z is  $NR^{16}R^{17}$ , the reaction, conveniently in the presence of a suitable base, of a quinazoline of the formula **VIII**:

$$L^{1} - (CR^{12}R^{13})_{p} = 0$$

$$R^{6} R^{5} R^{4} R^{2} R^{2} R^{3} R^{3} R^{3} R^{4} R^{2} R^{3} R^{3} R^{3} R^{4} R^{2} R^{3} R^{3} R^{3} R^{3} R^{4} R^{3} R^{3} R^{3} R^{4} R^{3} R^{3} R^{3} R^{4} R^{3} R^{3}$$

## VIII

wherein L<sup>1</sup> is a suitable displaceable group and R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>4a</sup>, R<sup>5</sup>, R<sup>5a</sup>, R<sup>6</sup>, R<sup>12</sup>, R<sup>13</sup>, X<sup>1</sup>, Q<sup>1</sup>, m, n and p have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with a compound of the formula **IXa**, or a reactive derivative thereof:

# H-NR<sup>16</sup>R<sup>17</sup>

## IXa

wherein  $R^{16}$  and  $R^{17}$  have any of the meanings defined in claim 1 except that any 10 functional group is protected if necessary;

and thereafter, if necessary:

- (i) converting a quinazoline derivative of the formula I into another quinazoline derivative of the formula I;
- (ii) removing any protecting group that is present by conventional means;
- 15 (iii) forming a pharmaceutically acceptable salt.